T-CELL VALUES (MEAN ±SEM) IN PATIENTS TREATED WITH BLOOD-DERIVED PRODUCTS

Group	% of total lymphocytes			OKT4/OKT8	% with OKT4/OKT8≤1·1
	OKT3	OKT4	OKT8		
Haemophilia A, severe					
Adolescents (n = 13)	71·0±3·7	34·2±3·7 (p<0·01)	33·8±3·7	1·1±0·2 (p<0·005)	46
Adults (n = 23)	74·2±2·0	31·5±2·9	37·2±3·4 (p<0·025)	0·8±0·1 (p<0·005)	74
Haemophilia A, mild (n = 3)	67·5±5·3	32·3±3·2	34·5±2·8	0·9±0·2 (p<0·05)	67
Classic von Willebrand's, severe (n = 3)	75·1±6·0	38·4±2·1	36·3±3·1	1·1±0·2 (p<0·05)	67
Patients on PCC					
Haemophilia B (n = 9)	65·6±3·2	46·0±4·8	28·2±2·2	1·9±0·2	11
Haemophilia A with antibodies to AHF (n = 3)	67·2±8·2	43·1±2·9	25·4±3·4	1·8±0·4	0
Chronic hypertransfusion states					
Sickle cell anaemia (n = 11)	66·4±3·2	41·5±4·0	30·9±3·6	1·3±0·1 (p<0·025)	27
Diamond-Blackfan syndrome (n = 3)	75·6±3·5	46·0±3·1	31·3±4·1	1·5±0·2	0
Congenital dyserythropoietic anaemia (n = 3)	78·0±7·0	48·0±3·0	30·0	1·4±0·1	0
Controls (n = 63)	69·3±5·9	44·7±1·7	29·5±1·6	1·8±0·1	10

complex concentrates ('Konyne') for circulating anticoagulants against antihaemophilic factor or for haemophilia B had normal T4/T8 ratios (table).

Lyophilised FVIII concentrate and prothrombin complex concentrates were examined for presence of thymosin,[10] which induces differentiation of T-cells[11] and stimulates lymphokine production.[12] No thymosin α_1 was detected in samples from five separate lots of lyophilised FVIII concentrate from two manufacturers; however, 1000 pg/ml thymosin α_1 was measured in samples from two separate lots of prothrombin complex concentrates. These immunological determinations[10] are comparable with concentrations in normal sera, but functional activities were not evaluated. We do not know whether thymosin in prothrombin complex concentrates protects individuals from the development of T-cell dysfunction, whether it reverses pre-existing imbalances of immunoregulatory T-cell activity associated with use of blood products, or simply whether the undefined agent(s) responsible for inducing T-cell dysfunction is absent in the material tested.

Repeated exposure to many blood products can be associated with development of T4/T8 abnormalities. Exclusion of lyophilised FVIII concentrates from the products available for the management of haemophilia A may reduce the incidence of AIDS, but the risk may not be eliminated altogether.

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AIDS IN HAEMOPHILIA PATIENTS IN SPAIN

SIR,—An acquired immunodeficiency syndrome (AIDS) has been observed in homosexual males, intravenous drug abusers, Haitian immigrants, and haemophiliacs.[1] We describe three haemophilia patients, treated with commercial concentrates of factor VIII, with severe opportunistic infections who are the first cases of AIDS in Spain. None of them were homosexual or drug abusers or had been under immunosuppressive treatment. Patients 1 and 2 were brothers.

Case 1.—9-year-old male. He had been in good health until 18 months before admission when he had frequent episodes of fever and cough with progressive weight loss. He was admitted for persistent fever in November, 1982. Physical examination revealed cachexia, oropharyngeal candidiasis, and acinar consolidation of right middle lobe in the chest X-ray. Laboratory data revealed severe lymphopenia, polyclonal hypergammaglobulinaemia, *Candida albicans* in urine culture and serological markers for previous infection by cytomegalovirus (CMV). He was anergic to skin-test antigens. Despite antibiotics and amphotericin B therapy the patient died of respiratory distress. Necropsy showed bilateral intra-alveolar haemorrhage with CMV and *Aspergillus* infection.

Case 2.—16-year-old male. He had good health until age 15 when he began to have fever, respiratory symptoms, diarrhoea, and weight loss. He was admitted in March, 1982. Physical examination revealed emaciation with oropharyngeal candidiasis, and a chest X-ray showed lesions which suggested bronchiectasis. As in case 1 there was severe lymphopenia and polyclonal hypergammaglobulinaemia. He also had disaccharidase deficiency (intestinal biopsy), oesophageal candidiasis (endoscopy), and serological markers for previous hepatitis A and B. With antibiotic and 5-flucytosine therapy the fever was controlled. Recently he has been readmitted, seriously ill.

Case 3.—38-year-old male. He had been in good health until June, 1982, when fever and progressive weight loss began. 1 week before his admission he had a generalised convulsive crisis, being sent to our hospital in February, 1983. He also complained of non-productive cough and increasing dyspnoea. Physical examination showed mental stupor without other neurological findings, herpes labialis, hepatosplenomegaly, and oropharyngeal candidiasis. Chest X-ray revealed a bilateral diffuse interstitial infiltrate and *Pneumocystis carinii* was identified from lung tissue and bronchial secretions. Other data were severe lymphopenia, polyclonal hypergammaglobulinaemia, serological markers for previous infections by Epstein-Barr virus, *Aspergillus*, *Candida albicans*, hepatitis A and B, and abnormal liver function tests with cirrhosis on needle biopsy. He was anergic to skin-test antigens. The

LYMPHOCYTE SUBPOPULATIONS IN PATIENTS AND CONTROLS

Case	SIG (B cells)	OKT3 (pan T)	OKT4 (T helper)	OKT8 (T suppressor)	OKT4/OKT8 (ratio)
1	27	50	9	52	0·17
2	46	38	9	35	0·26
3	4	86	20	64	0·31
Controls (n = 10)	9·5±3·5	81·5±6·6	55·0±4·4	26·6±5·4	2·1±0·3

SIG = surface immunoglobulin-bearing lymphocytes. Monoclonal antibodies studied by indirect immunofluorescence.
All results significantly different from control values at p<0·05 (Student's t test, quantile test for SIG) except for SIG and OKT3 in case 3.

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computed tomographic scan of the brain (CT) showed multiple hypodense lesions and the cerebrospinal fluid was normal. Combined co-trimoxazole and 5-flucytosine therapy stopped the fever, and his general condition improved. The lesions in the chest X-ray and brain scan have disappeared.

Lymphocyte subpopulation studies are summarised in the table, the most significant being the decrease of T helper/suppressor ratio. Both the clinical picture and the laboratory data accord with a diagnosis of AIDS.

Reports of AIDS in European homosexuals[2,3] point to the diffusion of AIDS beyond the USA, as do our own observations. Clinicians should be aware of the possibility of this syndrome in haemophiliacs who present with prolonged fever, respiratory symptoms, and weight loss. Other signs (lymphadenopathy, thrombocytopenia) are possible.

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PLASMA TRICYCLIC LEVELS: MISTAKEN IDENTITY

SIR,—In view of disagreement about whether or not tricyclic levels in plasma are clinically useful we would like to report the following two cases.

A 20-year-old outpatient with endogenous depression was prescribed nortriptyline 50 mg at bedtime. When seen 2 weeks later, she reported no improvement. A serum sample was obtained and assayed by high-performance liquid chromatography (HPLC). The sample contained no nortriptyline; instead, desipramine was found (37 ng/ml). When the patient was contacted by telephone, she stated that the medicine bottle, which had been filled by a pharmacy not affiliated with University Hospitals, was labelled "Nortriptyline, 25 mg—take two at bedtime". However, her description of the tablets' colour and markings indicated that they were desipramine. The patient was told to throw them away and to begin taking what were confirmed to be nortriptyline capsules. She soon became discouraged with her continued depression, however, and was admitted to hospital at her request.

A 31-year-old outpatient with schizoaffective illness was prescribed nortriptyline 100 mg at bedtime together with perphenazine 16 mg three times daily and amantadine 100 mg twice daily. When seen the following week, he reported feeling no better. A serum sample was obtained and assayed by HPLC. As in the first case, the sample contained no nortriptyline. Rather, desipramine was found (315 ng/ml). When contacted, the patient said that he thought that nortriptyline was the same thing as desipramine, which he had previously had prescribed without benefit. Accordingly, he had taken desipramine tablets, which he still had, instead of the nortriptyline capsules he had recently received from the pharmacy. He was told to dispose of the desipramine tablets and to start nortriptyline at a reduced dosage. At his next visit he appeared improved.

Measurement of plasma or serum tricyclic levels can be very helpful in indicating whether a patient's drug concentration is outside the therapeutic range, because of individual variation in metabolism, co-administration of drugs that affect the liver microsomal enzyme system, or non-compliance with the treatment regimen. As these cases illustrate, the assay can also alert the physician if his patient takes medication different from that which has been prescribed.

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CARDIAC ARRESTS IN GENERAL WARDS: THREE-YEAR FOLLOW-UP

SIR,—In 1982, editorials[1,2] questioned the need for more restraint in cardiac resuscitation in hospitals. I describe here the three-year outcome of an analysis of cardiac arrests on general wards.[3]

78 incidents of cardiac arrest occurred in Edinburgh Royal Infirmary over a six-month period. 34 (43%) of patients were resuscitated but only 11 (14%) were still alive at twenty-eight days. These 11 survivors have been followed up by scrutiny of medical records and deaths files. The patients' general practitioners were sent a questionnaire asking about the well-being of their patient and his quality of life and about whether the general practitioner felt that resuscitation had been appropriate. Quality of life was graded on a scale of grade 1 (excellent health) to grade 5 (very debilitated).

The 11 survivors were aged from forty-two to eighty-one. 5 of them were still alive at three years, 4 with grade 2 and 1 with grade 1 quality of life. The patient with grade 1 quality of life was aged eighty-one, which seems to support Bayliss' view[2] that age should not be a prime factor in deciding whether to resuscitate.

The patients who died were unwell between cardiac arrest and death. Peatfield et al[4] also found that protracted incapacity was associated with a poor prognosis.

In 3 cases the general practitioners felt that resuscitation had been inappropriate. However, 2 of these patients were found, subsequent to their cardiac arrest, to have disseminated carcinoma, and a third patient went on to acute renal failure and left-ventricular failure complicating subacute bacterial endocarditis. Although there is no formal "do not resuscitate" policy in Edinburgh Royal Infirmary, in no case could resuscitation be said to have been inappropriate in the light of the information available at the time of the cardiac arrest.

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OXYQUINOLINE NEUROTOXICITY

SIR,—Dr Rose (April 16, p 883) has not convinced us that our case-report (March 26, p 709) is neither an example of oxyquinoline neurotoxicity nor a case of subacute myelo-optic neuropathy (SMON). He ignores the fact that this case fulfilled the criteria for diagnosis established by the SMON Research Commission on the basis of 5839 patients in Japan.[5] Rose argues that cerebellar ataxia, poor memory, loss of temperature, unilateral scotoma, papilloedema, and improvement after drug withdrawal are not compatible with SMON. These objections are not relevant. Cerebellar ataxia is uncommon but possible, as confirmed by clinicopathological findings.[5] The feeling of poor memory was not related to mental deterioration as judged by psychometric tests but was related to obvious nervousness and anxiety which are common mental symptoms of SMON. Impairment of thermic sensibility has been observed with SMON.[5] Papilloedema was described in a patient taking oxyquinoline as long ago as 1966.[6] The small scotoma was unilateral but the optic neuritis was bilateral, as assessed by the angiographic and colour vision studies. The improvement after drug withdrawal in this case is not surprising: in Japan 46·2% of the patients had completely recovered six months after drug withdrawal.[5] We do think that this patient is an example of oxyquinoline neurotoxicity and a case of SMON.

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